REMARKS

Reconsideration of the allowability of the present application in view of the above amendments and the following remarks is requested respectfully.

Status of the Claims

Claims 1 and 30 have been amended. Claims 2, 3, and 29 have been cancelled without prejudice. Claims 34 and 35 have been added. The claims presently pending are Claims 1, 7 to 14, and 21 to 28, and 30 to 35.

Discussion of the Amendments

Claim 1 has been amended to more particularly define Hir as being a sequence encoding hirudin or a derivative thereof that is at least about 80% homologous to hirudin and to define protein(Y) as being a sequence encoding mini-proinsulin or a derivative thereof that is at least about 90% homologous to mini-proinsulin. Support for this amendment is in paragraphs [005] and [006] of the application and in Claim 2 as filed originally. In addition, while the application itself states that Hir is a sequence which encodes hirudin or a derivative thereof that is at least about 80% homologous to a natural isoform of hirudin, it is recognized that an isoform of hirudin is a polypeptide that slightly differs from hirudin and, therefore, a polypeptide that is at least about 80% homologous to a natural isoform of hirudin is a polypeptide that is at least about 80% homologous to hirudin.

Claim 30 has been amended to delete a phrase which has been made redundant by the above amendment to Claim 1, from which it depends ultimately.

Claims 34 and 35 have been added to more particularly define the nucleic acid recited therein. Support for these claims is present in the application at Examples 1 and 2.

No new matter has been added.

Summary of the Action

The present Action includes a rejection of all of the claims addressed by the Examiner, namely, Claims 1, 2, 7 to 14, and 21 to 33 (the only other claim which was then pending - Claim 3 - was withdrawn from consideration and is cancelled herein). The Action includes rejections under 35 U.S.C. §§ 102, 103, and 112. The rejections are discussed below.

Traversal of the Examiner's Rejection under Section 102(b)

The Examiner has rejected Claims 1, 7 to 14, 21, and 25 to 28 under Section 102(b) as being anticipated by the disclosure of U.S. Patent No. 5,434,073 to Dawson et al.

The Examiner's rejection is traversed respectfully.

Each of these claims distinguishes over the disclosure of Dawson et al. in that they define a nucleic acid in which the number of codons between S_x and Hir is, at most, 17 (15 codons for B_n, 1 codon for Z, and 1 codon for R). By contrast, as

discussed below, each of the relevant sequences disclosed by Dawson et al. includes at least 25 codons between the signal sequence (S_x) and Hir.

Dawson et al. discloses specifically only two nucleic acids which are relevant to the present invention, namely nucleic acids which encode a hirudin-containing fusion protein in which the sequence encoding the hirudin (the "Hir" sequence) appears in the 5' direction from the sequence encoding "protein(Y)". These sequences encode "Hirudin-IEGR-Hirudin" and "Hirudin-IEGR-Streptokinin". S_x is defined in the present application as being a nucleic acid which encodes a signal sequence or a leader sequence. Signal sequences and leader sequences are known to those of skill in the art to be sequences which participate in the localization of a polypeptide within a cell. In each of the relevant sequences disclosed by Dawson et al., "S_x" corresponds only to the "Pre" region of the α-factor pre-propeptide. "Hir" corresponds to the first hirudin-encoding sequence. The sequence encoding the entire α-factor pre-propeptide is 5' from the sequence encoding Hir and the nucleic acid encoding the "Pre" section of the α-factor pre-propeptide is 5' of the coding section of the peptide. The coding sequence of the α-factor pre-propeptide consists of 76 amino acids, or 25 codons. Accordingly, in the relevant nucleic acids disclosed by Dawson et al. there are at least 25 codons between the signal sequence (S_x) and Hir.

Given the above, none of the relevant sequences of Dawson et al. is a nucleic acid wherein the number of codons between S_x and Hir is, at most, 17. Dawson et al., therefore, does not anticipate applicant's claims.

In addition to the above, the present amendment to independent Claim 1, upon which the remaining rejected claims are dependent, further distinguishes the claims from the disclosure of Dawson et al. Claim 1 now incorporates the recitations of

Claim 2, which the Examiner has recognized as not being anticipated by the disclosure of Dawson et al. In summary, the claims now additionally distinguish over the disclosure of Dawson et al. in that they define a nucleic acid which encodes a fusion protein containing a hirudin amino acid sequence (or a derivative thereof) and a mini-proinsulin amino acid sequence (or a derivative thereof).

Traversal of the Examiner's Rejection under Section 103(a)

The Examiner has rejected Claims 22 and 24 as being rendered obvious by the disclosure of Dawson et al. in view of the disclosure of U.S. Patent No. 5,095,092 to Badziong et al. and Claim 23 as being rendered obvious by the Dawson et al. disclosure in view of that of Badziong et al. and further in view of the disclosure of Mead et al. The claims each define a process for using the nucleic acid defined by independent Claim 1.

The Examiner's rejections are traversed respectfully.

In each of the above rejections, the Examiner relies on the Dawson et al. primary reference as disclosing the production of a fusion protein using the nucleic acid of applicant's invention. As discussed above, however, Dawson et al. does not disclose the use of a nucleic acid of applicant's invention and none of the secondary references contains such a disclosure. As such, the disclosures of the combined primary and secondary references do not teach or suggest the subject matter of applicant's claims and, therefore, do not render the claims obvious.

Given the above, it is requested respectfully that the Section 103 rejections be withdrawn.

Discussion of the Examiner's Rejection Under the
Written Description Requirement of Section 112, First Paragraph

The Examiner has rejected Claims 1, 2, and 7 to 14 and 21 to 33 under the written description requirement of Section 112, first paragraph.

In the first instance, applicant notes that new Claims 34 and 35 have been drafted to define specifically the nucleic acids described in Examples 1 and 2 of the specification. According to the Examiner, claims defining such nucleic acids should satisfy the written description requirement.

The Examiner's rejection with regard to the remaining claims is traversed respectfully.

MPEP § 2163 states that "[t]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." The MPEP goes on to state that "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as [] by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention."

The claims have been amended to define the nucleic acid as encoding a fusion protein which includes hirudin (or a derivative thereof that is at least about 80% homologous thereto) and mini-proinsulin (or a derivative thereof that is at least about

90% homologous thereto). The basis of applicant's invention is the discovery that a fusion protein containing hirudin (or a derivative thereof) and mini-proinsulin (or a derivative thereof) may be exported from yeast with good yields. This identifying characteristic is well described throughout the application at paragraphs [0004] to [0014] and [0018] and in the Examples. The remaining elements of the nucleic acid (e.g., the promoter sequence, the signal or leader sequence, etc.) do not play a substantive role in defining the invention. Accordingly, the key identifying aspects of the present invention are now recited in each of the claims. Further, descriptions of the actual reduction to practice with respect to a nucleic acid encoding such a fusion protein are contained in Examples 1 and 2. Methods for using the same are described also in Examples 3 to 7.

Given the above, there exists adequate description of an actual reduction to practice and of identifying characteristics respecting the subject nucleic acid to show to one skilled in the art that applicant was in possession of the claimed invention.

Discussion of the Examiner's Rejection Under the
Enablement Requirement of Section 112, First Paragraph

The Examiner has rejected Claims 1, 2, 7 to 14, and 21 to 33 under the enablement requirement of Section 112, first paragraph. According to the Examiner, applicant has not enabled one skilled in the art to practice, without undue experimentation, various embodiments which are encompassed by the claims.

In the first instance, applicant notes that new Claims 34 and 35 have been drafted to define specifically the nucleic acids described in Examples 1 and 2.

According to the Examiner, claims defining such nucleic acids should satisfy the enablement requirement.

The Examiner's rejection with regard to the remaining claims is traversed respectfully.

The claims have been amended to define a nucleic acid which encodes a fusion protein that contains a hirudin amino acid sequence or a derivative thereof (hereafter, collectively, a "hirudin" sequence) and a mini-proinsulin sequence or a derivative thereof (hereafter, collectively, a "mini-proinsulin" sequence) and a process for using the same. It is applicant's position that one skilled in the art can practice applicant's invention, as defined in the amended claims, without undue experimentation. Factors to be considered in determining whether undue experimentation is necessary are summarized in *In re Wands* as follows: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the invention; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention.

The nature of the present invention is that it relates to a nucleic acid which encodes a fusion protein comprising hirudin and mini-proinsulin sequences. The claims, as amended, define specifically such a nucleic acid.

The state of the prior art is that it discloses a nucleic acid which encodes a hirudin-containing fusion protein (but not the present fusion protein). The level of one skilled in the art in this area is that such a person would know what promoter sequences, signal sequences, leader sequences, linker sequences, and untranslated

sequences, etc. can be used in the expression of the fusion protein. The inventor has provided direction regarding what hirudin derivatives may be used in the practice of the present invention (see, for example, paragraph [032] of the application) and working examples exist to describe how to construct such a nucleic acid (see Examples 1 and 2) and how to use it (see Examples 3 to 7).

Given the above, applicant submits that one skilled in the art will be able to practice the present invention without undue experimentation. Accordingly, the claimed invention is considered to be enabled. If the Examiner persists in an enablement rejection of the amended claims, it is requested respectfully that he explain why one of skill in the art would not be able to practice the present invention. Such explanation would give the applicant an understanding of the Examiner's position; this in turn should help accelerate the prosecution of the application.

Discussion of the Examiner's Rejections Under Section 112, Second Paragraph

The Examiner has rejected Claim 17 under Section 112, second paragraph, because he considers the terms "hirudin", "hirudin derivative", "natural hirudin isoform", "mini-proinsulin", and "lepirudin" to be indefinite.

The Examiner's rejection is traversed respectfully. "Hirudin" is a specific protein whose sequence is well known to those of skill in the art. "Hirudin derivative", as recited in the claims, is a derivative that has at least 80% homology to hirudin. One of skill in the art would know which sequences fall within this scope and the application states that homologies may be calculated using a certain program (see paragraph [007]). The Examiner's objection to the term "natural hirudin isoform" has been rendered moot by the deletion of this phrase. "Mini-proinsulin" is defined in the

application as being insulin with a shortened C-chain (see paragraph [006]). Mini-proinsulin is further discussed in Irish Patent No. 62511 (copy available upon request), an English language equivalent of European Patent No. 0 347 781 (cited in the application at paragraph [004]). "Lepirudin" is the generic name for "Refludan®" (see paragraph [003] of the application as amended) and "Refludan®" is known to have the sequence of Leu-Hirudin (see paragraph [036] of the application).

Discussion of the Provisional Obviousness-type Double Patenting Rejections

The Examiner provisionally rejected Claims 1, 2, and 31 under the doctrine of obviousness-type double patenting as being unpatentable over Claims 2, 4, 5, and 25 of U.S. Application No. 10/076,634 and Claim 2 of U.S. Application No. 10/076,631.

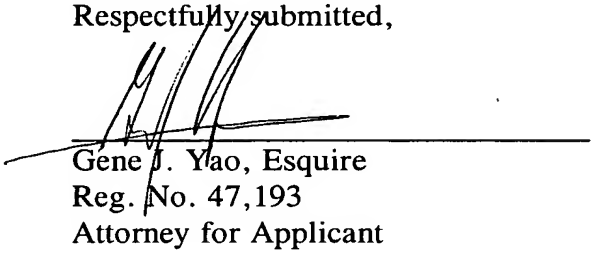
The Examiner's rejections at present are merely provisional as no patent upon which an obviousness-type double patenting rejection may be based has yet issued. Accordingly, it is submitted that no response is required at the present time.

Conclusion

In view of the above amendment and remarks, applicant requests respectfully that the Examiner withdraw his rejections.

An early and favorable reconsideration of the rejections and an early and favorable allowance of all of the pending claims are requested respectfully.

Respectfully submitted,



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